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DOCUMENT-IDENTIFIER: US 6379675 B1
TITLE: Immunological combination compositions and methods

Brief Summary Text (42):
Helicobacter pylori is the spiral bacterium which selectively colonizes human gastric mucin-secreting cells and is the causative agent in most cases of nonerosive gastritis in humans. Recent research activity indicates that H. pylori, which has a high urease activity, is responsible for most peptic ulcers as well as many gastric cancers. Many studies have suggested that urease, a complex of the products of the ureA and ureB genes, may be a protective antigen. However, until now it has not been known how to produce a sufficient mucosal immune response to urease without cholera toxin or related adjuvants.

Brief Summary Text (43):
Antigens or immunogenic fragments thereof stimulate an immune response when administered to a host. Such antigens, especially when recombinantly produced, may elicit a stronger response when administered in conjunction with adjuvant. Currently, alum is the only adjuvant licensed for human use, although hundreds of experimental adjuvants such as cholera toxin B are being tested. However, these adjuvants have deficiencies. For instance, while cholera toxin is a good adjuvant, it is highly toxic. On the other hand, cholera toxin B, while non-toxic, has no adjuvant activity. It would thus be desirable to provide immunological compositions capable of eliciting a strong response without the need for an adjuvant.

Brief Summary Text (44):
In certain instances when multiple antigens (two or more) are administered in the same preparation or sequentially, a phenomenon called efficacy interference occurs. Simply, due to the interaction of one or more antigens in the preparation with the host immunological system, the second or other antigens in the preparation fail to elicit a sufficient response, i.e., the efficacy of the latter antigen(s) is interfered with by the former antigen(s). It would thus be desirable to provide multivalent immunological compositions which do not give rise to this efficacy interference phenomenon; for instance, without wishing to necessarily be bound by any one particular theory, because the second antigen is a lipoprotein and as such is having an adjuvanting effect on the first antigen and, when in a combination composition with an adjuvant, a synergistic potentiating effect is obtained (whereby the first antigen is not interfering with the second antigen and vice versa).

Brief Summary Text (55):
Moreover, it has also surprisingly been found that administration to a host of at least one antigen, at least one lipoprotein and, optionally an adjuvant by either co-administration or by sequential administration (over a suitable time period such that each of the antigen, adjuvant and lipoprotein are present within the host at the same time) obtains an immunological response to the antigen by the host. This immunological response is generally better than that obtained by administration of the antigen alone or by administration of the antigen and adjuvant. Lipidated proteins appear to stimulate the immune response, in the manner of the adjuvant cholera toxin B.

Brief Summary Text (69):
The adjuvant can be any vehicle which would typically enhance the antigenicity of the antigen, e.g., a suspension or gel of minerals (for instance, alum, aluminum hydroxide or phosphate) on which the antigen is adsorbed; or a water-in-oil emulsion in which antigen solution is emulsified in mineral oil (e.g., Freund's incomplete adjuvant), sometimes with the inclusion of killed mycobacteria (e.g., Freund's complete adjuvant); or cholera toxin (sometimes with cholera toxin B, which may

enhance the effect); or, any of the other adjuvants known in the art, or discussed in the Background of the Invention. The antigen and/or the lipoprotein can be absorbed onto or coupled with the adjuvant.

Drawing Description Text (7):
FIG. 5 is a graphical representation of the immune response of mice immunized twice, intranasally, with jack bean urease, either above or with OspA or cholera toxin, as measured in an anti-urease ELISA at day 9 after the second immunization.

Detailed Description Text (34):
Plasmid pBluescript KS+ (Stratagene) was digested with XbaI and BamHI and ligated with a 900 bp XbaI-BamHI DNA fragment containing the complete coding region of B. burgdorferi strain ACA1 ospA gene, to form a lipoprotein fusion vector pLF100. This procedure is shown schematically in FIG. 1 of application Ser. No. 08/475,781, filed Jun. 7, 1995 and incorporated herein by reference.

Detailed Description Paragraph Table (7):
Anti Ure Anti Osp Spots/ Spots/ .mu.g 10.sup.6 Cells 10.sup.6 Cells .mu.g Jackbean Ure OspA Route IgA IgG IgA IgG -- 1 L .sup. i.n. n.d n.d 583 345 -- 1 NL i.n. n.d. n.d 4 2 20 -- i.n. 11 0 n.d. n.d 20 1 L .sup. i.n. 189 18 742 257 20 10 L .sup. i.n. 191 39 1237 174 20 + CT 10 .mu.g -- i.n. 478 42 n.d. n.d. 20 -- i.n., 0 1 25 0 i.g. 20 10 L .sup. i.n., 322 31 1919 177 i.g. i.n. = intranasal i.n., i.g. = intranasal & intragastric (the indicated dose was given by each route) L = lipidated OspA; NL = non-lipidated OspA CT = cholera toxin (10 .mu.g CTB + 10 ng CTX/mouse (PMSV)) n.d. = not determined